THE TREATMENT OF SYPHILIS

BY

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The editor of the *British Journal of Dermatology* has kindly honoured me by a request to write my experience of the treatment of syphilis. I think this wish is best met by a *resumé* of actual practice at the Royal Herbert Military Hospital, Woolwich, a large garrison, where I have been working for the past three years. It may also prove of interest to give a short history of the underlying factors which have been chiefly instrumental in causing a very marked reduction of syphilis within the British Army in recent years. Prophylaxis by medical treatment necessarily reacts on civil communities, and a reduction in the amount of disease in the Army means the lessened incidence of syphilis in civil communities, whilst the converse holds equally true.

The time to commence mercury in the treatment of syphilis is a crucial question and involves many considerations. Mr. Jonathan Hutchinson states: "If the patient has never had syphilis before, whatever are the characters of any primary sore which he may exhibit, the chances are two to one that the sequel will prove that it contained the germs of true syphilis." If this were true we would be justified on a probability of averages in prescribing the drug at once in every case of venereal sore. In the British Army, in England and abroad, where numerous cases of venereal sore come under early notice, soldiers are first treated in hospital. Commencing, however, from September, 1903, men, on discharge from hospital, remain under continued observation. Exact diagnosis is thus more feasible than in civil life where cases are wholly treated as out-patients, where their actions are uncontrolled, and where they commonly communicate disease to others. I conducted an investigation in 1904, at Cairo,

amongst 200 consecutive in-patients with venereal sores. The cases on discharge from hospital were kept under prolonged observation. There were forty-five cases of syphilis, that is, a relative frequency of 3·5 non-infecting chancres (soft chancres) to 1 of syphilis.* Previous and present experience and carefully collected military statistics support this view. Naturally it is a hard point to estimate accurately, as soldiers, more especially in England, may resort to civil practitioners and chemists in order to avoid loss of pay by reason of admission to hospital. No doubt many cases are only sent to Mr. Hutchinson when there is a strong probability of syphilis. I think, therefore, on the evidence, that the probability of chances in a large number of cases is about three to one against syphilis. The relative frequency, however, is of slight value in arriving at a correct diagnosis, the nature of the chancre and the condition of the adjacent lymphatic glands being of the utmost importance as regards treatment. In the foregoing investigation at Cairo, which I have since verified at Woolwich in many hundreds of cases, induration in some degree was almost invariably present at some time in syphilitic chancres, although it need not necessarily be obvious on the occasion or occasions on which the medical man happens to see the case, since it may have disappeared, or may not have developed. The induration should be felt with the fingers. It is rapidly dissipated by adequate treatment with mercury, and is much more marked in some cases, especially on the tense corona glandis. It is commonly less marked and frequently overlooked on the frænum. In the soft substance of the glands or on the external skin of the penis it may be absent, or not appreciable (parchment induration). Induration was, with rare exceptions, also present in the proximal lymphatic glands in the primary stage, and these glands were usually bilaterally enlarged as the rash came fully out. There was either a discrete bullety enlargement or hyperplastic non-suppurating mass (bubo), which rarely ended in suppuration in the case of syphilis, and the amygdaloid or bullet nature of the individual glands could be later made out as the mass slowly subsided under mercurial inunctions. These hyperplastic mattings in the groin usually resulted from concealment, irritation, and active exercise in the chancre stage. In the case of non-infecting sore, sup-

* *Syphilis in the Army*, 1907, John Bale, Sons & Danielsson, Appendix I.

purating buboes rapidly resulted from concealment or neglect in the initial stages. The demonstration of *Treponema pallida* of Schaudinn in the chancre is proof of syphilis, but Ducré's bacillus, the cause of non-infecting chancre, might also be present in a mixed syphilitic infection. The condition of pseudo-chancre indurè first described by Fournier, in Paris, is a condition where induration is stated to occur in a chancre which is non-syphilitic. The fact of the nearest lymphatic glands being normal will usually clear the diagnosis. It is feasible that in some instances such a condition may occur in a person already the subject of constitutional syphilis, being, in fact, a local inflammatory reaction. Although I have in very rare instances seen conditions that might be so described, yet from their extreme rarity I prefer to suspend judgment for a while. In the light of recent observation I am of opinion that induration in a chancre (Hunterian chancre) or in the resulting cicatrix is the most valuable clue we have to the recognition clinically of early syphilis, especially in association with bullet glands. If, therefore, we can properly exclude a condition such as the above, it considerably advances our knowledge of a difficult subject. Acquired syphilis on the genitals is nearly always accompanied with ulceration, and in certain phases of the ulcer it is quite impossible from the local appearance to diagnose syphilis. Induration may occur early or late in the base or edges of the ulcer, but when slight may escape our vigilance. In the case of artificially inoculated syphilis on the skin by vaccination or otherwise, a papule is the usual initial lesion, and in rare instances I have seen such occur on the glans penis. The vast majority of syphilitic ulcers, however, probably come under the category of so-called "mixed" infections, the ulceration, purulent products, and in phagedæna the active necrosis or even sloughing of tissue being mainly dependent on accidental factors, such as neglect, exercise, and the irritation of a tense prepuce. It can therefore be readily understood why suppurating buboes occur in connection with syphilis, and in fact they are by no means rare. Further, I also quite frequently see a true attack of gonorrhœa later followed by syphilis the patient first developing a chancre after some time in hospital. Scars on the penis are very dangerous criteria on which to diagnose syphilis, as the largest scars are often due to a loss of substance in a non-infecting chancre with phagedæna. Scars on the penis without

any collateral evidence are not infrequently accepted as proof positive of syphilis by writers on nervous diseases, but statistics compiled on such slender data should be rejected. Both non-infecting and infecting chancres may be indolent in healing, and the incidence of appearance after connection is frequently a doubtful criterion on which to base a diagnosis, since truthful histories are hard to elicit and syphilitic chancres are commonly due to "mixed infections." The time limits were worked out many years ago on experimental or vaccinal inoculations, being ten to forty days, with an average of twenty-five days. Although syphilitic chancres are in the large majority of instances single, yet the non-infecting variety of chancres also frequently appear single, more especially in hospital, where auto-inoculation has been prevented by aseptic or antiseptic treatment. Amongst patients presenting multiple sores, balanitic excoriations, or abrasions, one of these may later prove to be syphilitic, or a ring of induration may develop from the whole excoriated surface. Urethral chancres usually occur at the meatus with urethral discharge, and may prove to be erosive in nature; induration occurs in most cases as the ulcer heals, and both chains of inguinal glands are usually implicated. Erratic chancres are very rare, and are almost invariably syphilitic. The most common situations are the lip and tonsil. I have seen one, however, on the centre of the forehead, and one on the calf of the leg. The nearest lymphatic glands are usually typical. Metchnikoff claims to have successfully inoculated the *Treponema pallida* and prevented syphilis by the early application within twenty-four hours from contagion of an ointment of calomel 10 parts and lanoline 20 parts. The use of soap or vaseline prior to coitus and washing with any antiseptic lotions immediately afterwards are also of great prophylactic value and have been long recognised. Any oily substance would tend to block the minute orifices by which the micro-organisms gain an entry, and also tend to lessen the risk of abrasions caused by coitus. Cauterisation rapidly converts an unhealthy sore into a healing ulcer, stops phagedæna, tends to limit bubo formation, and expedites recovery. The application of a caustic does not in reality alter the nature of an infecting sore, and the condition of the adjacent lymphatics nearly always comes to our rescue. Further, a rash occurs in syphilis, whether the chancre is cauterised or not. I consider that non-infecting sores (soft chancres), if unhealthy looking or discharging,

should be locally touched with pure carbolic acid, which is comparatively painless, on admission and every third day, according to the indication of the particular case. Chancres, unless phagedænic, need not be touched if obviously indurated, or undoubtedly syphilitic, or if they bleed profusely before and after touching, since such bleeding, as in simple inflammation, is a sign of commencing resolution. A perchloride of mercury dressing (1 in 2000) is useful, and iodoform is very valuable. Balanitic sores or abrasions often heal better with a solution of Argent. nitratis gr. ij to the ounce on lint. If phimosis co-exists, hot baths, and packing under the foreskin with carbolised gauze, and stretching with phimosis forceps may suffice; if not, operation is necessary. Primary circumcision, except in phimosis associated with gonorrhœa, is, I think, bad practice, as the whole wound commonly becomes infected, and the duration in hospital may extend to three months. It is best to make a dorsal incision of the prepuce, let the wound heal, and treat the syphilis. When the wound has healed and the thickening subsided a secondary circumcision should be done. Buboes in the groin are usually due to irritation caused by the chancre rubbing against the prepuce or clothes, and hence exercise should be avoided in the early stages. Suppurating buboes should be incised and scraped at an early date, as otherwise they are apt to burrow extensively, especially in cachectic subjects, or in hot climates, and so necessitate extensive operation accompanied by profound debility. Many writers have advised the withholding of mercury in cases of phagedæna. I admit that caution and judgment are necessary. Local treatment, free exposure, prolonged baths, diet, and stimulants ordinarily suffice for phagedænic ulcers, except when the nearest glands are typical of syphilis, when mercurial inunctions should be used. The two common causes of phagedæna are phimosis, congenital or inflammatory, and neglect by the patient. Sloughing of the soft tissues rapidly occurs owing to the highly infective pus being pent up. Mr. Jonathan Hutchinson states that phagedæna only occurs in syphilis. It occurs, however, in both non-infecting and infecting chancres. I have collected a large series of cases in both. A lowering treatment has unquestionably a bad effect, whether dietetic or medicinal, especially if mercury is given when syphilis is non-existent.

The grave effects of syphilis are largely due to the original

intonsity of infection, to personal susceptibility to the action of the virus from lowered general health, from whatever cause arising, to racial susceptibility, to intemperate habits, to the neglect of early treatment, and to the injudicious use of mercurial preparations. The primary and early secondary stages run a definite course, and no line of treatment can absolutely prevent the evolution of manifestations, but good treatment in hospital in the early stages markedly ameliorates the general blood condition and better guards against later relapse and tertiary manifestations. Kaposi says that "treatment in the primary stage disorders the evolution of the symptoms of infection and makes tertiaries more frequent." In my experience it is only when treatment is not given because the syphilis is not recognised, when mercury is injudiciously administered, especially in the form of insoluble grey oil, or when remedies are too early suspended, that tertiaries become frequent. In cases of malignant syphilis, however, which are fortunately rare, tertiary manifestations may occur within six months, concurrently with the initial secondary rash. In the case of venereal sores, which do not present the classical features of syphilis, administration should, I think, be deferred until two of the accepted signs of syphilis are present, namely, evident induration of the chancre, which is present at some period in probably 90 per cent. of infecting chancres, and indurated enlargement of the proximal lymphatic glands. These are most valuable indices to syphilis before the occurrence of rash or other symptoms. I always treat clear cases of infecting chancre with a course of forty inunctions of ung. hydrarg. before the rash begins and then wait for further symptoms, which occur in a modified degree in the case of syphilis. It is frequently stated as a justification for withholding mercury in the primary stage (*i. e.* before rash appears) that the evolution of secondary symptoms is thereby unduly delayed. I do not think that this is appreciably so, although the local evidence of induration in the chancre or lymphatic glands is rapidly dissipated, but I do think that the ensuing disease is considerably modified by a course of forty inunctions in the primary stage, that the general health suffers less with the later advent of the rash and sore throat, and that relapses, tertiaries, and nervous lesions are subsequently much less. I exclude malignant syphilis from this category. In those fortunately rare cases where the induration of the chancre or lymphatic glands is not at some time

apparent, it is wiser to wait for further evidences of constitutional syphilis, such as rash, sore throat, mucous patches, alopecia, etc., which ordinarily occur within four months or so of infection. If syphilis is definitely diagnosed the patient is then more willing to undergo the prolonged treatment which is essential to cure. This latter consideration more especially applies to civil practice, as the patient usually prefers a definite diagnosis. Personally, I decline to give a diagnosis in doubtful cases under four months, and experience demonstrates the wisdom of reticence. The early, non-infiltrated, roseolar, erythematous syphilide (also called rubeolar syphilide in that type of it which resembles measles), which is very common in syphilis, may only last four days to one week, and is commonly overlooked by both patient and medical man. Owing to the naturally evanescent nature of such rashes various new forms of treatment have from time to time been unduly lauded. After the first nine months external manifestations are rare both in treated and untreated syphilis, which shows the active part played by Nature, apart from our remedies, in the process of repair. In an experience of over a thousand cases thoroughly treated in hospital in the chancre stage by mercury, diet, and every resource at present known to the profession, secondary symptoms, *i. e.* rash, sore throat, mucous patches regularly occurred in some degree. The evolution of these symptoms could not with certainty be prevented, although unquestionably modified. I cannot, therefore, endorse Mr. Jonathan Hutchinson's statement that "I never expect to see secondary symptoms now if I have seen the case before we begin."* Severe papular or pustular eruptions, with or without iritis, or albuminuria, are ordinarily due to severe infection with syphilis, to absence of treatment, and to inadequate treatment, such as grey oil. It is necessary to be more stringent in dealing with such patients than with the general run of cases who have a mild ephemeral roseolar rash, or sore throat and slight glandular enlargements. Patients with severe lesions, if robust, usually stand mercury well, especially by the inunction form. For such cases three courses of forty inunctions ung. hydrarg. B.P. in doses of 1 drachm in the

* *Second Report of Advisory Board on the Treatment of Venereal Diseases in the Army*, 1905, p. 10.

first nine months is, I think, essential, daily warm baths and free dietary being almost as important as the drug treatment.

At Woolwich some 1000 or more venereal cases are annually admitted as in-patients. The local garrison is 5000 strong, and numerous cases also come from the adjoining London garrison, 4000 strong, also colonial foreign invalids, and men on furlough from other stations. Syphilis in all stages comes under close observation, but more especially the initial and secondary lesions. A contrast between the effects of treatment in civil and military communities is unfair to the former. In the Army, excluding foreign invalids, we ordinarily deal with picked healthy adults. The men are well housed, well clothed, and well fed. When sick they are treated in the early and more remediable phases of disease as in-patients in hospital under the best hygienic conditions and with an ample dietary, a most important consideration in dealing with syphilis. The treatment ordered is carried out by specially trained orderlies under the daily supervision of an officer. In civil life, in hospital practice on the other hand, the patient continues at his work, and the above conditions can rarely be fulfilled since there are only some fifty beds in the whole of London (a city of 5,000,000 inhabitants) for the in-patient treatment of venereal diseases. As a result of this defect, venereal disease is sown broadcast amongst the population, and the resulting insanity due to syphilis is dealt with in lunatic asylums maintained at immense cost by the State. Further, the out-patients have not the means to buy good food, and they ordinarily live under very bad hygienic conditions. They take their medicine or not as they please, and whilst frequently forgetting their treatment, too rarely forget the temporary stimulus afforded by alcohol in the local gin-shops, which naturally accentuates their disease and preserves their syphilis. Venereal diseases should be notifiable, and cases treated as in-patients for a period of one to two months in the communicable stages. In better-class private practice the patient commonly essays to conceal the origin of venereal disease from the doctor, and naturally desires to keep the fact of its existence from his friends and relatives. In military practice concealment, when detected, is an offence with penalties. The medical man in civil practice is consequently forced to accommodate himself to the circumstances of the individual case, and treatment may thus be unfairly

crippled, or too frequently has to be made subservient to the convenience and caprice of the individual patient. I fully realise the difficulties of the situation, but do not agree with Colonel Lambkin, R.A.M.C., "that our great hospitals make no attempt at curing"; * that "in ninety-nine cases out of a hundred in England at the present day the treatment is one of symptomatic amelioration, and generally speaking no real attempt is made to deal with the disease." †

The Augean stable has first to be cleansed by a better system and a few legal enactments. Our great hospitals may bring a man to their out-patient clinics, but they cannot make him drink his medicine or admit him for treatment. The reduction of syphilis within the Army in recent years is mainly dependent on treatment in hospital, and on the adoption of a valuable system of "out-patient" control and supervision throughout the whole British Army, with a continuance of treatment for two years and observation for a further year. In July, 1903, I forwarded to the War Office some printed matter published in India in 1901 to show the absolutely fundamental importance of collecting accurate statistics of syphilis, and so ensure the more exact diagnosis of non-infecting chancre (soft chancre) and infecting chancre (syphilis), since adequate treatment necessarily implies the accurate diagnosis and recognition of early syphilis. The statistics of venereal disease in the British Army in the past have been commonly rejected at international congresses, etc., owing to their inaccuracy. I further suggested that a strict record of re-admissions to hospital for relapse of syphilis should be accurately kept, in order to verify the curative value of various forms of treatment, and finally, that as the neglect of adequate treatment of syphilis, especially in the early stages (first six to nine months), was a principal factor in perpetuating the disease, that the purely symptomatic treatment should entirely cease, and that prolonged out-patient treatment and supervision should later supplement hospital treatment in the Army in order to prevent relapse and consequent re-admission to hospital. The above suggestions, fully set forth in the preface to my recent book,‡ were given effect to by the War Office, who put forward a temporary scheme in September,

* *The Hospital*, June 29th, 1907. Reprinted in the *Journal R.A.M.C.*

† *Ibid.*

‡ *Syphilis in the Army*, 1907. London: John Bale, Sons & Danielsson.

1903, for the more accurate diagnosis of syphilis and soft chancre, and arranged, by Army Order 158 of September, 1903, for the regular out-patient attendance of soldiers. This Army Order, which has had a world-wide effect, was later embodied in the King's Regulations, paragraphs 1080, 1174, and provides that "soldiers temporarily unfit, but for whom treatment in hospital is not essential, will attend at the hospital or inspection-room as directed by the medical officer. They will not be permitted to leave barracks, and will be excluded from the canteen. They will be relieved from all duties or employed on light duties and fatigues according to medical recommendations." The pay warrant also provides that a soldier who is physically inefficient from venereal disease or its effects forfeits service pay, which is restored to him on return to ordinary duty when considered efficient by his commanding officer. In January, 1904, the results of the previous scheme proving favourable, a permanent scheme—"Instructions regarding Procedure in Cases of Syphilis"—was taken into force throughout the Army in England and abroad wherever British troops were stationed. These instructions were later embodied into Appendix VII, Regulations for Army Medical Services. Briefly, these instructions contain the suggestions set forth in July, 1903, and also arrange for a syphilis case-sheet for every man, which is transferred with him. Statistics are rigidly collected and individual initiative stimulated, whilst the results of treatment are tabulated. The reduction of venereal disease in the British Army has thus been enormous, and the good results have reacted also on the civil community, but there is plenty of scope for more thoroughly detecting and treating early venereal disease, both amongst soldiers and civilians.

I have given the above history in some detail, as an inference has been recently made by Colonel Lambkin, R.A.M.C., whereby the brilliant results latterly obtained in the British Army were attributed to the particular method of administering mercury, so strongly advocated by him, of treating soldiers by intra-muscular injections of mercurial preparations, such as grey oil (Lambkin's cream).* Although the grey oil treatment was introduced about 1891 the marked reduction in the Army has only occurred during the past five years or so in England, and in India since the control of diseased women

* *Journal R.A.M.C.*, May, 1908, p. 559; replied to in the July, 1908, number of the same journal.—H. C. F.

commenced in the year 1898 onwards. In 1897, amongst the British Army in India, syphilis reached the highest ratio on record, namely, 106 admissions per 1000 men, whereas in 1903 it was only 46 per 1000, and yearly less ever since. In 1896 to 1899 in India I, in common with other officers, used soluble perchloride of mercury injections and mouth treatment for out-patients, whose attendance at that time was not compulsory as it now is, since September, 1903. I found these soluble injections valuable. Brilliant results, therefore, are mainly due to the control of diseased women in India, and to the careful treatment of soldiers in hospital in the initial stages of disease, which lessens the local spread of disease by imperfectly treated soldiers, to continuance of treatment as out-patients, and to the united efforts of Army Medical Officers over a series of years rather than to any special mode of treatment, such as insoluble grey oil, or other mercurial preparation. During the past fifteen years my work has been almost exclusively confined to treating venereal diseases in large military stations at home and abroad. During this period I have extensively tried most of the recognised modes of administration, by the mouth, by inunctions, by injections, and by calomel vapour baths. In early syphilis—that is, during the chancre and early rash stage—and before the disease has become established, I am firmly convinced that both the mouth and inunction methods of administering mercury in suitable and average cases are infinitely preferable as regards curative action on syphilis, to the injection of insoluble salts, such as grey oil. I have given some thousands of these intra-muscular injections and recorded the results in order to study the relative effect both on in-patients and out-patients. During the past year at Woolwich I have conducted a close research on this point. I find that when inunctions of ung. hydrarg. B.P. are judiciously used, the induration of the chancre and of the lymphatic glands is much more rapidly and thoroughly dissipated, and that a gain of several pounds is the rule and not the exception. I have found severe relapses and loss of weight to be much more common after the use of insoluble grey oil, the lymphatic glands are not nearly so beneficially affected, syphilitic nervous lesions are more common, and soldiers have to be re-admitted to hospital.*

* Confirmation of these conclusions is to be found in an article by Capt. Dorgan R.A.M.C., in the *Journal R.A.M.C.* for August, 1908.

In the army, in the case of in-patients who are necessarily in hospital in the chancre and rash stage, we are chiefly concerned in trying to arrive at what best holds the syphilis in check. In the garrison of 5000 men, in the year 1903, at Woolwich, the intra-muscular injections of insoluble grey oil were ordinarily used. There were 477 admissions for syphilis, which included many relapse cases, the average number of men daily sick in hospital with syphilis being 54. In 1904, intra-muscular injection of mercury was used for in-patients, but owing to the inauguration of the rigid out-patient system from January, 1904, already outlined, there were only 331 admissions for syphilis, the average number of daily sick in hospital being 56. In October, 1905, I initiated inunctions of ung. hydrarg. and baths for in-patients, weekly grey oil injections being reserved for out-patients. There were 202 admissions for syphilis in 1905, average daily sick being 30. In 1906 there were 129 admissions for syphilis, and the average number of daily sick was 13, the strength of the garrison being 4500 men. These good results accrued from the number of re-admissions for relapse and the number of daily sick being reduced, owing to more efficacious treatment whilst in hospital in the early phases of the disease. In 1907 there were 87 admissions for syphilis, the same practice continuing. In 1908 the average number of in-patients for syphilis is 9 in a garrison of 4500 men, at the date of writing—August, 1908. Further, in 1905 there were some 150 men attending weekly as "out-patients" for syphilis. The average number of out-patients attending weekly during the present year is 61. This reduction amongst out-patients is also due to more effective in-patient treatment in the early phases of disease by inunctions of mercury, baths, and full dietary. Cases which have not received thorough inunction or mouth treatment whilst in hospital in the early chancre or rash stage very commonly relapse and have to be re-admitted to hospital. Naturally there are a very large number of cases of syphilis which present very slight skin or mouth manifestations at any period of their syphilis, and grey oil injections in such cases have obtained a quite undeserved amount of credit. In severe cases, in obstinate skin or mouth lesions, the curative action of insoluble grey oil is frequently not apparent, and in order to dispel the lesions I am commonly obliged to adopt other methods. Amongst the 87 admissions for syphilis in 1907, no less than 22 were cases of relapse occurring in

men whilst out-patients under active mercurial treatment by intra-muscular injections of insoluble grey oil.

Lang, of Vienna, "first introduced grey oil in 1886. He objects to intra-muscular injections as these are more liable to be followed by complications."* Lang commonly uses the inunction method. Lafay, of Paris, modified Lang's formula. Dr. Althus, of London, introduced grey oil into England. Colonel Lambkin in the British Army has used it since 1891, at first using Dr. Althus's cream. Lambkin's formula, "especially in its later form, closely resembles the grey oil of Continental writers."† I question the "slow absorption and elimination" of insoluble salts of mercury as set forth by Colonel Lambkin,‡ since both are reported to have been sufficiently uncertain, rapid, and irregular to cause mercurial poisoning in well authenticated cases, and even deaths due to this method are recorded in Surgeon-General Fawcett's article on Egypt.§ Other deaths and cases of poisoning are recorded.‖ The fact of accumulation of insoluble salts of mercury at the site of injection is largely owing to the introduction of insoluble material into muscles primarily intended by Nature for locomotion. The salt, therefore, is not regularly absorbed, and may be suddenly eliminated. Further, there is no premonitory warning or adequate means of control as with other safer methods, when mercurial stasis occurs, and this dangerous condition is naturally apt to occur more frequently with insoluble salts. It is common knowledge that mercury, like arsenic, has a cumulative action in the body, so that it is not so much the intake as the output that we must look to. This may explain the bad results with atoxyl. The consensus of English opinion in civil practice is strongly adverse to the use of insoluble salts of mercury for intra-muscular injection. Dr. A. Whitfield, London, "considers the use of insoluble preparations such as grey oil as hardly justifiable in

* *Third Report of Advisory Board on the Treatment of Venereal Diseases in the Army*, p. 29.

† *First Report of Advisory Board on the Treatment of Venereal Diseases in the Army*, p. 16.

‡ *Journal R.A.M.C.*, May, 1908, p. 558. Replied to in the July, 1908, number of the same journal.

§ *First Report of Advisory Board on the Treatment of Venereal Diseases in the Army*, Appendix A, p. 64.

‖ *First Report of Advisory Board on the Treatment of Venereal Diseases in the Army*, p. 27.

view of the recorded deaths from this method of treatment."* Mr. Charles Gibbs, London Lock Hospital, states that "severe relapses are twice as frequent after injections as after inunctions or pill treatment, and iritis is peculiarly common in the relapse after intramuscular injection."† Other experts state that "it decimated their clinics." Mr. Arthur Ward, in revising the records of the Lock Hospital, London, says "he was struck by the numbers of patients who only took one injection and never came again."‡ Mr. Jonathan Hutchinson does not consider "it so good as the administration of grey powder."§ Dr. Radcliffe-Crocker remarks: "From a study of the literature of the subject it seems that the dangers from insoluble preparations are considerably greater than those from soluble, and if salivation once sets in you have no controlling power over it at all."‖

The foregoing independent testimony, contained in the *Second Report of the Advisory Board on the Treatment of Venereal Disease in the Army,* is that of a committee specially appointed to go into such matters, the views being those of leading experts in London.

The following research work which I undertook for the War Office in 1905–6 on three samples of mercurial cream kept at uniform temperatures in an incubator may prove of interest. The research is mainly of a chemical nature, but the therapeutic action of insoluble grey oil in the treatment of syphilis has been closely watched during the past three years.

Mercurial Cream.

	A. For temperatures 70° to 80° F.	*B.* For temperatures 80° to 95° F.	*E.* For temperatures 90° to 105° F.
Hydrarg. pur . . .	2 drachms (by weight)	2 drachms (by weight)	2 drachms (by weight)
Adeps lanæ anhydrous .	3 drachms (by weight)	3 drachms (by weight)	3 drachms (by weight)
Paraffin Liquid, Carbol. 2 per cent. ad .	10 drachms (by measure)	—	—
Paraffin Molle, Alb. Carbol 2 per cent. ad	—	10 drachms (by measure)	—

5 minims contain 1 grain of metallic mercury.

Dose, 5 minims.

* *Second Report of Advisory Board on the Treatment of Venereal Diseases in the Army.*

† *Ibid.* ‡ *Ibid.* § *Ibid.* ‖ *Ibid.*

Report on Three Samples of Mercurial Cream.

A form.—When exposed to a temperature of 70° to 80° F. the metallic mercury separated out and sank to the bottom. If the pot is placed in boiling water and stirred the mercurial cream in *A* form is fit for use in three minutes, and remains so for fifteen minutes, when it requires heating again. This form readily passes through the needle. The three samples of this form have been used.

B form.—When exposed to a temperature of 80° to 95° F. the metallic mercury separated out and sank to the bottom as in Form *A*. When *B* form is placed in boiling water the mercurial cream is fit for use in five minutes, and remains so for ten minutes if taken out of the hot water, when it requires heating again. This form is not so soluble as *A*, and apparently more suitable for climates warmer than England. The three samples of *B* form have been used.

E form.—When exposed to a temperature of 90° to 105° F. the metallic mercury separated out as in *A* and *B* forms.

When *E* form is placed in boiling water the mercurial cream is fit for use in eight minutes, and will only remain so for five minutes if taken out of the hot water. If used in this country it requires to be kept in hot water the whole of the time when in use. It is extremely insoluble, and difficult to get it to pass through the needles except when nearly boiling—probably not suitable for even tropical use. It was necessary to stop using it before the sample bottles had been finished. The "chronic intermittent" plan of intra-muscular injection has been used with all three forms—that is, six weekly injections of gr. j Hg., rest for three months, then six weekly injections, and so on for two years. I have not seen any case of mercurial stomatitis under the use of the "chronic intermittent" plan. Owing, however, to the frequency and persistence in many instances of marked glandular enlargement amongst out-patients, and the not infrequent occurrence of severe relapse, the total effect on the early stages of syphilis of "insoluble" salts of mercury is not always apparent amongst out-patients. I have not seen a single case of nodosity or abscess result from any of the forms *A*, *B*, or *E*, and this is solely due to asepsis and care. With *E* form, however, apart from the insolubility, several men stated that it made them feel very ill. This is attributed to the accumulation in the tissues at the site

of injection, and sudden elimination, but largely accentuated by beer drinking, irregular habits, and smoking whilst out-patients. The foregoing report was made two years ago. I have studied the action of grey oil to date (August, 1908), and the effect on syphilis is, in my opinion, of a negative character.

At Woolwich, the method of inunction which I use for in-patients is on the general lines of Aix-la-Chapelle, modified by service conditions. I substitute barley-water for sulphurous spring water in order to assist elimination by the kidneys and to guard against albuminuria—which is rare in syphilis, except in severe cases which have not come under notice early, or have not received adequate treatment. The method requires the daily supervision of an officer, orderlies are trained, and patients instructed how to use the glass rubbers either on themselves or on one another. Soldiers, as a general rule, are not too weak to do all that is requisite. The patients use condemned hospital flannel underclothing, which is changed once a month and then destroyed—so the cost is very slight. A hot bath, with plenty of soap and water, is used every morning before the inunction, which latter lasts half an hour, and takes place at 10 a.m. The skin looks like blacklead when the ointment has been thoroughly rubbed in. Forty inunctions of 1 drachm ung. hydrarg. B.P. compounded with lanoline or ung. paraffin flav. 1 drachm, or other substances, form a course. Each man is provided with the exact measured quantity. I omit the inunctions on Sundays. After twenty to twenty-five inunctions when thoroughly done the teeth may, in some instances, especially if at all carious, feel tender on eating. I usually stop for a week and give potass. iodidi in doses of gr. x, three times daily, and then finish the course. In severe cases it is wiser to give fifty to sixty inunctions with judgment. All carious teeth should be attended to prior to the commencement of a course. A mouth wash of acetate of alum is used in each case during the inunction course every two hours by day, and a soft tooth-brush is used twice daily. The groins and armpits are closely shaved, and must be kept so in order to guard against mercurial pustulation, which can usually be obviated by care and attention. I select the groins, inner sides of thighs, and armpits owing to the greater frequency of glandular orifices in these situations and so better regulated absorption, as well as for the fact that the

glands in these situations are ordinarily much enlarged and must be reduced before there is any question of suspending vigorous mercurial treatment. The glands are no doubt the repositories of syphilis, and when thoroughly reduced are capable of asserting their normal depurative and other functions. In early syphilis the glandular tissue of the tonsils is ordinarily first hypertrophied and congested, although later in the disease the tonsils may atrophy or disappear. As cases of syphilis vary so much in variety and intensity, no hard and fast rules can ever be laid down as to treatment. One man may require mercury, another food, another tonics. I find no other method of treatment in the initial chancre and rash stage, say the first six months from contagion, that is so generally valuable as inunctions, but the method requires experience and detailed personal attention. I think that a syphilised person should always receive two courses of forty inunctions within the first six to nine months, and if practicable four courses in the first eighteen months. After the first two courses mouth treatment will ordinarily suffice to guard against relapse. Hydrarg. cum creta with opium in small doses, as recommended by Hutchinson, acts well in guarding against relapse, alternating with tonics, potass. iodidi, or other remedial measures according to the particular indication or the individual case. In many cases hydrarg. cum creta will fulfil all necessary requirements throughout the case, but in the light of later experience I believe that I am more thoroughly treating syphilis by using the inunction method with daily bath whenever practicable in early syphilis. According to the evidence of the Advisory Board reports inunctions are used in the French, German, Austrian, Bavarian, and other armies as the routine method of treating syphilis. The method is in use at Aix and Wiesbaden and at other clinics on the Continent. It can be understood, however, that the excellence of this method can only be tested amongst in-patients under restrictions, such as exist in military life—and that in civil hospital practice, or private practice, this treatment may be difficult to arrange. Mouth treatment is ordinarily only used on the Continent to guard against relapse—and to meet the convenience of patients—just as in the British Army grey oil injections are largely used for convenience and to meet the service requirements of out-patients. In the late secondary and tertiary stages administration by the mouth acts well of preparations,

such as liquor hydrarg. perchlor. in combination with potass. iodidi, or the biniodide of mercury in solution, as the digestion is not at this period so easily disturbed as in the initial congestive stage of syphilis. Grey powder with opium acts well in the primary and early secondary stage, and is strongly advocated by Mr. J. Hutchinson. Opium is a valuable ally with mercury, as it checks diarrhœa and promotes diaphoresis. Mr. Hutchinson considers that inunctions are very valuable, but that grey powder is more convenient for private practice. Calomel vapour baths are best suited to severe external lesions such as marked papular or pustular lesions and ulcerating gummata, which may resist other methods. They should not be too long continued, as mercurialisation may be rapidly induced owing to the large extent of skin surface from which absorption is taking place. I employ Lee's vapour bath in all severe cases, either with or without calomel, according to the necessities of the individual case. I usually give about ten baths, the baths taking place every other day with ½ drachm of calomel for each bath. The drug must not be wiped off from the body. The Zittmann treatment, which consists of mercury in minute doses administered in a small room in which the patient remains, was well thought of by the late Sir Alfred Cooper, and the method is fully discussed in his work on syphilis. It is suitable for cachectic emaciated cases or cases of malignant syphilis who do not react to ordinary remedies. A room for this class of case is being built at Woolwich and at Rochester Row, London. Some foreign invalids, who weigh only six to seven stone, are unable to take any specific treatment, or eat ordinary food. The reported results in malignant syphilis are very favourable, as much as a stone in weight being put on. Hot-air electric baths would no doubt serve the same purpose. The patient must be built up first and local measures are essential. No doubt change of air is of great value, but general treatment is equally important in all grave cases. Milk, eggs, and port wine should supplement the ordinary diet. The duration of administration of mercury is in some measure dependent on the type of constitutional disease, on idiosyncrasy, and on the general health of the patient. I object to any method of pushing the drug and making the patient fit in with the treatment. I have seen men broken down by mercury as well as by syphilis, and this condition may be most difficult to put right, and it is then not easy to convince the patient

that the remedy is of value. If the drug be given until the gums are touched, mercurial poisoning may easily occur. This danger is largely guarded against by the prior treatment of carious teeth by astringent gargles, such as acetate of alum, and by daily hot baths. If mercurial stasis occurs, and a blue line appears on the gum, or if the gums be spongy and the tongue swollen, stop the drug at once. Give soft food and stimulants, hot baths, paint the gums with a solution of gr. x to the ounce argent. nitratis, and give a weak permanganate of potass. gargle every hour. It is my practice to give mercury more vigorously in the first than in the second year. If the patient is robust, and the attack severe, as evidenced by an infiltrated papular or pustular rash, with or without iritis or alopecia, and marked glandular enlargement, a larger quantity of mercury in the early stages is well tolerated by a carefully dieted patient in hospital. If, on the other hand, the infection is a mild one, as evidenced by a non-infiltrated roseolar rash and slight adenitis, or if the patient is nervous or debilitated from any cause, or has carious teeth, a much smaller dose may be badly borne. As a rule mercury should be efficiently, invariably, but intermittently given for twelve months, although the first nine are much the more important, with gradually increasing longer intervals in the second year, and combined with mixed treatment with potass. iodide or tonics during the intermissions according to the general condition. No hard and fast rule as to dosage can ever be laid down which would suit every case, but the merits of each must be absolutely decided by the experience of the individual practitioner.

Owing to our ignorance of the laws of assimilation and elimination it is unwise to give the patient in any stage as much mercury as he can stand, because this practice, though advocated by some persons, constitutes an abuse of the drug, and may result in mercurial stomatitis, or mercurial stasis and poisoning, from at first being unduly accumulated and later too suddenly eliminated. This would affect the general health, which is a most important consideration, as the manifestations of syphilis are usually in inverse ratio to it. Treatment should, I think, be directed towards enabling the patient to take the drug by regulating elimination, and inducing an increase of metabolism by baths, food, and general exercise in the fresh air. If the bactericidal properties in the blood are to effect the cure of syphilis, this must necessarily result

from increased metabolism due to the careful administration of mercurial preparations. As a result of such administration the lymphatic glands become reduced in size and so continue their depurative and eliminatory function. When they fail they break down and suppurate. This result is not infrequently seen in neglected or badly treated syphilis. Too long a continuance of a large dose in any form creates a markedly retrograde effect, and gives rise to anæmia, loss of weight and general condition, as well as acting as a systemic poison, and probably prevents anti-bodies forming in the blood. The factor "general condition," when adequately maintained, has no doubt as powerful an effect as the mercury in improving the status of the red blood-corpuscles, and in eliminating the syphilis by improving the tone of eliminating organs, such as the liver, kidneys, and skin. "If blood-counts be made it will be found that the count of red cells and the amount of hæmoglobin increase during the first three weeks of mercurial treatment begun when secondary manifestations of syphilis have occurred. After that time if mercury is still given the hæmoglobin and, later, the number of red corpuscles begin to decline" (Cabot). Hydro-therapeutics and electro-therapeutics are useful adjuncts to a mercurial course, and a valuable complement after it. The absence of cachexia of the face is a valuable index to the progress of the case and a guide to interrupting or continuing the mercurial course. The weight is probably proportionate to the condition of the blood and to the satisfactory nature of our remedies, since great variations are often apparent in the weight of untreated and properly treated cases of syphilis. In severe cases, treated or otherwise, the weight may fall steadily for a time, and anæmia is more or less marked. A fat person, however, may lose weight and yet gain in general condition. The persistence of indurated and enlarged lymphatic glands is a most valuable sign for the continuance or otherwise of a brisk mercurial course, especially by the inunction method combined with radiant light baths, or of a substituted mixed treatment. Until the induration and enlargement of the glands is thoroughly and permanently reduced in cases of constitutional syphilis there can be no question of cessation of treatment. Under efficient treatment these glands are reduced to normal in about six to nine months from the date of infection, but in some cases this can occur earlier, and quite independently of treatment. The lymphatic glands are ordinarily normal

with tertiary lesions if we except early malignant syphilis. Intramuscular injection of insoluble grey oil is not nearly so efficacious in reducing glandular enlargements as other methods, such as inunction or hydrarg. cum creta in the early stages. Slight albuminuria occurring as the direct result of syphilis is not a bar to the carefully watched administration of small doses of mercury, but a large amount of albumen in the urine, or albuminuria the result of nephritis from other causes, is a contra-indication to the use of the drug. Mercury is often badly borne in syphilis associated with recent malaria, scurvy, or tubercle, or in any grave anæmic state. Nervous tremors occurring during the mercurial course contra-indicate the continuance of the drug.

Alcoholic subjects and persons with neurasthenic temperaments, epileptic fits, or hereditary tendency to insanity require great care. Cellulitis not infrequently attacks wounds or alcoholic syphilised subjects under active mercurial treatment, and sepsis may quickly occur after operation in the early stages. Boils, whitlows, and carbuncles not infrequently occur in association with early syphilis. Grave septicæmia may occur with necrosis of bone in tertiary phases, and treatment should be first directed to ordinary surgical procedure for the necrosis and secondarily to specific drugs.

Before iodide of potassium is administered the question of renal sufficiency should be adequately gauged. If albumen is present, or the quantity of urine insufficient, the iodide eruptions are likely to occur, and hence the value of free dilution of the drug together with hot air or electric light baths, as these exercise a markedly beneficial effect on the kidneys, and assist elimination by the skin. The headache and osteoscopic pain of early syphilis may rapidly yield to potassium iodide alone, or in combination with mercury, and a pustular syphilitic rash is markedly benefited. The drug may give rise to headache if albumen is present in the urine.

Potassium iodide is more obviously beneficial the further the stage from primary infection, and its use, therefore, is imperative in the late secondary and tertiary stages, or in any manifestations, however early, such as malignant syphilis presenting the attributes of those stages. This drug is most valuable in cases of early syphilitic orchitis, in periostitis, nodes, gummata, gummatous ulcerations, and in threatened brain or cord lesions. Patients who are intolerant of

small doses, such as gr. v, may take a larger one with impunity. The drug is best borne about an hour after meals in dilute solution in such vehicles as water, milk, and sarsaparilla. The depressant action is best avoided by prescribing it for short periods at a time of ten to fourteen days, and in solution with ammonia carbonate, also by associated tonic treatment and hot-air baths, and by administering the large dose at bedtime and avoiding its use in the early morning. It is then not so likely to derange digestion or cause depression. A course of a month once a year is valuable as a precautionary measure against parasyphilitic affections, and is strongly advocated by Sir William Gowers. The drug, as a matter of routine, should always be given as the complement of the mercurial course, since it is generally believed to assist in the gradual elimination of the accumulated mercury, and so guard against mercurial stasis and poisoning. It also acts, especially when combined with sarsaparilla, by relieving the liver and kidneys, which may be chronically congested or lardaceous. The drug can remove the barricades of nascent fibrous tissue in which the syphilitic virus or its toxin is no doubt lodged in latent and later stages, and thus permits the leucocytes to enter and effect the removal of the virus or its products, and this explains the lessened anæmia of the patient in suitable cases. The drug often rapidly reduces the enlarged glands. The moderate use of the drug, therefore, causes a more healthy tone of tissues, blood, lymphatics and organs, which can then more naturally overcome the effects of the bacillus or its toxin. In certain stages of threatened brain syphilis which have been neglected in the early stage mercury may prove more valuable, but commonly in "syphilis grave" or in "malignant" syphilis mercury may prove quite useless, and general condition is the first consideration.

"As a result of the apparent beneficial effects which had been obtained from the use of atoxyl in sleeping sickness, it was suggested by Uhlenhuth that this drug might also prove successful in syphilis, the latter being, like sleeping sickness, a protozoal disease."* Atoxyl has given rise to many cases of toxic poisoning as well as to many cases of total blindness in treating sleeping sickness. This is attributed to adulteration of the drug, etc., but the symptoms appear to be those of ordinary arsenical poisoning, namely "gastro-intestinal

* *Brit. Med. Journ.*, August 15th, 1908, pp. 391–394.—Col. Lambkin, R.A.M.C.

pains, nausea, vomiting, painful micturition, and painful sensations in the limbs" (*i. e.* arsenical neuritis),* these symptoms possibly being due to intra-muscular injection as can occur with insoluble injections of mercury. Soamin (sodium-aminophenylarsonate), soluble in five parts of water, is a preparation made by Burroughs Wellcome & Co., London. It is reported to have a toxicity of one fortieth that of arsenious acid and to be a safer drug than atoxyl. It contains 22·8 per cent. of arsenium (As) in organic combination. The use of arsenic in the treatment of syphilis and other skin-diseases is extremely well known. In the British Pharmacopœia, Donovan's solution (liquor arsenii et hydrargyri iodidi), has been prescribed for many years in treating syphilis, and patients gain weight on it. I commonly use it, and it is valuable in certain cases. I quite concur in the view that arylarsonates may "exert their use in strengthening the phagocytic defence of the host."† Judicious dietary, iron, quinine, sanatogen, malt and cod-liver oil in common with arsenic exert a similar effect. I do not, on the evidence presented, concur in Colonel Lambkin's view, "that one important fact has been established, that is, that in these salts (arylarsonates) we are now in possesion of a *specific* for syphilis, and the importance of this cannot well be exaggerated.‡ In the very next sentence it is stated, "that they do not kill the germ as mercury is supposed to do."§ Apparently thirty cases in all were treated by Colonel Lambkin with the arsenical salt soamin, but only thirteen of the "most prominent" are recorded. These thirteen cases were admitted to hospital with the initial lesions of syphilis for soamin treatment in April and May, 1908, and discharged from hospital in May and June. Up to July 30th, 1908 (the date of writing), in a period of under four months' observation no relapse is reported to have occurred. On such evidence the statement is made "that injections of soamin can be looked on as prophylactic in the majority of cases against any further development of the disease (syphilis) if given early and in sufficient quantities."‖ It is necessary to remember that external manifestations in the average run of cases are comparatively rare a year from infection both in treated and untreated syphilis. This fact is generally recognised by writers on this subject. Further, tertiary symptoms, when they occur, usually do so in three

* *Ibid.* † *Ibid.* ‡ *Ibid.* § *Ibid.*

‖ *Brit. Med. Journ.*, August 15th, 1908, pp. 391–394.

to five years after infection. The fact of the thirteen "prominent" cases gaining four to six pounds whilst treated in hospital by soamin for some time is very largely due, in my opinion, to the admittedly beneficial effect of rest and a generous full hospital dietary, namely "ordinary," as well as to local treatment in the early and more remediable stages of syphilis. Average cases of syphilis have a spontaneous tendency to cure under such highly favourable circumstances quite apart from treatment by drugs. I have seen ten to thirty pounds in weight thus gained even in severe cases without a grain of mercury or arsenic being used. At the present time there is a severe case in hospital at Woolwich who has gained thirty pounds within two months on general and local treatment, and numerous recorded cases can be cited of a gain of half to one stone, where previously treatment by specific drugs has been repeatedly tried and failed. How true this is in speaking of malignant syphilis is a matter of general knowledge.

Quinine in dilute acid solution is often most valuable precedent to, or after, the first mercurial course in cachectic cases. Whether it exerts a specific action on the *Treponema pallida* as on the malarial parasite is uncertain, but I always temporarily substitute it for mercury if there is an associated malarial history or if syphilitic fever is present. As early syphilis is associated with a loss in numbers of the red blood-corpuscles and in the amount of hæmoglobin in these cells, quite possibly its chief action may be in overcoming the degenerative action, and thus assist the blood to deal with the inroads of the virus in the early and more remediable phases of the disease by increasing its phagocytic power, or by the formation of anti-bodies. Cod-liver oil and iron are similarly valuable for their hæmatinic powers. Any drug, however, or any means which tends to reduce the number of spirochætes in the system in the early stages will consequently lessen the amount of toxin produced which can later injure the central nervous system and give rise to parasyphilitic affections.

The very greatest advantage may accrue from a cessation of mercury or potass. iodide, and the substitution of other tonic remedies. I think that this is more especially the case in alcoholic, scorbutic, anæmic, or tubercular subjects, and in malignant syphilis. There is no class of disease in which the beneficial results of judicious and early treat-

ment are so marked as in syphilis. If the remedy used is doing good the result is early apparent, and the manifestations of the disease disappear; if, on the contrary, the manifestions are stationary or growing progressively worse the remedy is inadequate and fresh methods should be essayed, either by an increase or decrease of dose, or the substitution of other drugs and remedies. The application of the rules of antiseptic, aseptic, and general surgery to the wounds of syphilis is valuable in proportion to the extent and manner in which they are used. If there are ulcers in the throat or mouth local treatment is requisite, and a minced meat or stew diet is essential to successful results. Otherwise the patient tends to lose weight if he is unable to masticate or swallow too solid food, and mercury would only aggravate matters. Success more often depends in maintaining the strength by means of the judicious use of stimulants and nutritious food than on drugs. This is especially true in cases of iritis, severe throat lesions, necrosis of bone, and in malignant syphilis.

I have merely endeavoured to suggest some of the general principles and broad lines on which the various forms of treatment may be best conceived and best maintained.